1093-36 Myocardial Blood Flow in Patients With Anderson-Fabry Disease and Cardiac Involvement

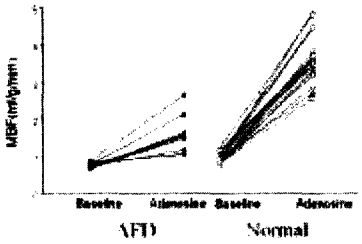
Bhavesh Sachdev, Heiko Kindler, O. E. Rimoldi, Philip Lee, Rajesh Thaman, William J. McKenna, Perry M. Elliott, Paolo G. Camici, St. George's Hospital Medical School, London, United Kingdom, MRC Clinical Sciences Centre, Imperial College School of Medicine, Hammersmith Hospital, London, United Kingdom

Background: Cardiac involvement is common in Anderson-Fabry disease (AFD) and patients (pts) may present with angina despite angiographically normal coronary arteries. To assess the function of the coronary microcirculation in pts with AFD, we measured myocardial blood flow (MBF) and coronary vasodilator reserve (CVR) using positron emission tomography (PET).

Methods: Nine normotensive, hemizygous male AFD pts (56.3±11.7 yrs) and 18 sex and age-matched controls (50.2 ± 6.0 yrs, p=ns vs AFD) were studied. Six pts were in NYHA class II or above. Pts had history of chest pain (n=6), palpitations (n=7) or syncope (n=2). MBF was measured at rest and during adenosine-induced hyperemia using $H_2{}^{15}O$ and PET. CVR was calculated as adenosine/resting MBF.

Results: All pts had an increased left ventricular mass index (244 ± 78.9g/m^2). Resting (0.72±0.09 vs 0.90±0.13 ml/g/min, p= 0.002) and hyperemic MBF (1.64±0.49 vs 3.62±0.66 ml/g/min, p<0.001) were lower in pts compared to controls. CVR was significantly blunted in pts (2.27±0.53) compared to controls (4.06±0.8, p<0.001). No significant relation was found between CVR and the degree of left ventricular hypertrophy.

Conclusion: CVR is substantially reduced in patients with AFD and its reduction is unrelated to left ventricular mass index. In the absence of coronary artery disease this suggests diffuse coronary microvascular dysfunction, which may contribute to ischemia and explain anginal symptoms.



1093-37 Effect of Hypoxia on Coronary Microcirculation in Coronary Artery Disease Patients

Christophe A. Wyss, Pascal Koepfli, Mehdi Namdar, Gregory Fretz, Magdalena Seebauer, Christian Schirlo, Philipp A. Kaufmann, Cardiovascular Centre, University Hospital, Zurich, Switzerland

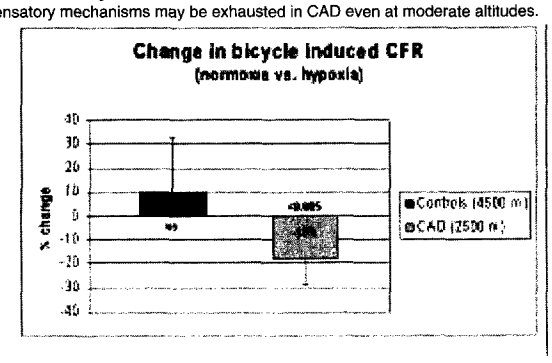
Background: There are poor data on the influence of high altitude on myocardial blood flow (MBF) and coronary flow reserve (CFR) in healthy humans and CAD-patients.

Aim: To assess the influence of acute exposure to a simulated altitude of 2500m above sea level in CAD patients and 4500m in healthy male volunteers on MBF at rest and during bicycle exercise (Ex) vs. adenosine (Ado) induced hyperemia.

Methods: 15O-labelled H2O and PET was used to measure regional MBF (ml/min/g) at rest, during Ado (0.14mg/kg/min over 7 min) and after supine bicycle in 8 CAD patients and 10 controls under normoxic conditions. 30 minutes later all MBF measurements were repeated during inhalation of a hypoxic gas mixture (oxygen-concentration:16.3% in CAD, 12.5% in controls).

Results:Resting MBF increased significantly during hypoxia in both groups (1.1 ± 0.2 vs. 1.4 ± 0.3, p<0.01 control, 1.2 ± 0.2 vs. 1.4 ± 0.2, p<0.05 CAD). The exercise induced flow increase was significantly larger during hypoxia in controls (1.9 ± 0.3 vs. 2.6 ± 0.6, p<0.0001) but remained unchanged in CAD (2.5 ± 1 vs. 2.5 ± 1, ns),whereas workload at comparable rate pressure product decreased significantly in both groups (-28%, p<0.0001 in controls,-11%, p<0.05 in CAD). This results in a significant decrease in CFR in CAD at moderate altitudes in contrast to a trend to increased CFR in controls at higher altitudes.

Conclusions: The significant decrease in exercise-induced CFR in CAD indicates that compensatory mechanisms may be exhausted in CAD even at moderate altitudes.



1093-38 Feasibility of Exercise Rubidium-82 Positron Emission Tomography Myocardial Perfusion Imaging

Benjamin J. Chow, Terrence D. Ruddy, Mary M. Dalipaj, Robert A. de Kemp, Charles Nadeau, Heikki Ukkonen, Karthikeyan Ananthasubramaniam, Rob S. Beanlands, University of Ottawa Heart Institute, Ottawa, ON, Canada

Background: Vasodilator stress is widely used with positron emission tomography (PET) perfusion imaging for the diagnosis of coronary artery disease. However, exercise stress may provide functional information helpful to clinical decision-making and may be preferred by patients wishing a non-pharmacologic approach. Because of the short half-life of Rb-82, transmission imaging for attenuation correction can be carried out following stress emission imaging.

Methods: We evaluated treadmill exercise stress using the Bruce protocol as an alternative to dipyridamole stress in 22 patients (mean age 62 years ± 10 years, 20 males) with intermediate or high pre-test probability for coronary artery disease. Stress testing was carried out with rest transmission and emission imaging followed by exercise or dipyridamole stress and then stress emission and transmission imaging. Perfusion defects were quantitatively measured using a 70% threshold and expressed as %LV.

Results: Angina was more common (p=0.035) with dipyridamole stress (11/22 patients) compared to exercise stress (5/22 patients). ST segment depression was more common (p=0.003) with exercise stress (10/22 patients), compared to dipyridamole stress (6/22 patients). Defect size with stress was similar (p=NS) with exercise (13.8 ± 16.0%), compared to dipyridamole (12.9 ± 15.8%). Defect size at rest was also similar (p=NS) on the day of exercise (4.8 ± 8.9) vs dipyridamole stress (3.8 ± 6.2). The sizes of the stress defects following exercise vs dipyridamole stress were highly correlated (r=0.85, p=0.0001) and also at rest (r=0.94, p=0.001). Imaging quality defined as target to background ratio was similar (p=NS) following exercise stress vs dipyridamole stress.

Conclusion: Exercise Rb-82 PET myocardial perfusion imaging is highly feasible and provides imaging results of diagnostic content and quality similar to dipyridamole stress

1093-39 Glucose Intolerance and Obesity Alter Myocardial Metabolism in Young Women

Linda R. Peterson, Alan D. Waggoner, Pilar Herrero, Susan Racette, Tim Meyer, Lisa de las Fuentes, Samuel Klein, Victor G. Davila-Roman, Robert J. Gropler, Washington University, St. Louis, MO

Background: Obesity is associated with cardiac dysfunction and increased risk of cardiovascular death with women being at higher risk than men. Results of studies in animal models of obesity have shown that worsening glucose intolerance, associated with obesity, is paralleled by increasing myocardial fatty acid uptake (FAUP), fatty acid utilization (FAUT), and fatty acid oxidation (FAOX), which are linked to destructive processes including myocardial apoptosis and free radical generation. The impact of obesity and glucose intolerance on myocardial fatty acid metabolism in humans is unknown. **Methods:** We studied 21 healthy women: 9 lean and 12 obese (mean ± SD, body mass index 22 ± 2 kg/m^2 and 36 ± 6 kg/m^2, respectively). All were normotensive, nondiabetics, non-hyperlipidemic, & had a normal echocardiogram. All had a screening 2-hour glucose tolerance test from which the area under the curve (AUC) for glucose, a measure of glucose intolerance, was calculated. After a 12 hour fast, myocardial blood flow, oxygen consumption, and fatty acid metabolism (FAUP, FAUT, FAOX) were measured by positron emission tomography (PET) using O-15 water, C-11 acetate, & C-11 palmitate, respectively.

Results: Plasma fatty acid levels, myocardial blood flow & oxygen consumption did not differ between the 2 groups. The obese women were older (30 ± 5 vs. 24 ± 4 yrs, p<.01) and had a higher AUC (14298 ± 2099 vs. 11884 ± 161, [mg/dL x min] p < .02). BMI correlated with AUC (r=.65, p<.005). FAUP correlated with BMI (r = .47, p < 0.5). FAUP, FAUT, and FAOX all correlated with AUC: r = .75, p < .0002; r = .67, p <.002; and r = .64, p < .005, respectively.

Conclusions: Increasing obesity and worsening glucose intolerance are associated with an increase in myocardial FAUP. Consistent with experimental models of obesity, increasing glucose intolerance results in increased myocardial FAUP, FAUT, and FAOX. Although requiring further study, these findings support the theory that increased fatty acid metabolism may lead to cardiac dysfunction in young obese women.

1093-40 Myocardial Efficiency Is Unimpaired in Type 1 Diabetes Mellitus

Muthayyah Srinivasan, Pilar Herrero, Janet B. McGill, Alan D. Waggoner, Victor G. Davila-Roman, Robert Gropler, Washington University School of Medicine, Saint Louis, MO

Background: Cardiovascular disease is the most lethal complication of patients with type 1 diabetes mellitus (DM). Although DM can result in left ventricular (LV) systolic and diastolic dysfunction, the impact of DM on LV energy transduction is unknown. **Methods:** We studied 18 DM (39±11 yrs, 6 males) and 18 normal individuals (28±5 yrs, 7males). All subjects were healthy normotensive nonsmokers without coronary artery disease by stress testing. Myocardial oxygen consumption (MVO_2 µmol/gm/min) was measured by PET and ^{11}C-acetate. Myocardial minute work (MW) per gram of LV mass (LVM) was measured by echocardiography as product of systolic blood pressure (SBP) * cardiac output (CO = LV outflow tract (LVOT) velocity x LVOT area x heart rate (HR)) and then divided by LVM. Both MVO_2 and MW were converted to energy equivalents (Joules/gm/min). Efficiency was calculated as a ratio of (MW/MVO_2)*100%. **Results:** DM subjects tended to have a higher MW due to a higher HR and SBP. In addition DM subjects had a significantly elevated MVO_2 compared with normals. Both groups had similar efficiency (see table). **Conclusions:** Type 1 diabetes mellitus is associated with normal myocardial